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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,948	READ ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *172-209* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *172-209* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/3/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/3/04 has been entered.

2. Claims 172-209 are currently pending and are being examined in this application.

Information Disclosure Statement

3. The references in the information Disclosure filed on 3/3/04 have been fully considered and entered into the application.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 172-184, 186, 188-192 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

The written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure or some combination of such characteristics.' *Enzo Biochem,Inc. v. Gen-Probe Inc., 296 F 3d. 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002).*

The instant claims briefly recite a method of synthesizing a polypeptide array, wherein said array comprises at least two different polypeptides immobilized on a substrate, comprising: a) contacting said surface with a first protected amino acid; b) contacting the said surface with a second protected amino acid; and c) repeating the above steps until at least two different polypeptides are formed at known location on said substrate surface.

The specification description is directed to the use of photo lithographic techniques in the methods of making arrays of chemical compounds such as peptides or oligonucleotoides, which clearly do not provide an adequate representation regarding the open ended method of synthesizing a polypeptide array of the instant claims. And the use of photolithographic technique is critical or essential to practice the instant invention.

With regard to the description requirement, applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)

(bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

"Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor can not lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods." *Cf. University of Rochester v. G.D. Searle & Co., Inc., Monsanto Company, Pharmacia Corporation, and Pfizer Inc. No. 03-1304, 2004 WL 260813 (fed. Cir., Feb. 13, 2004).*

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound or methods of making the compounds or arrays; which requires a representative sample of methods of making the compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

Additionally, the narrow scope of examples directed to photolithography technique in making arrays are clearly not representative of the scope of the claimed method of synthesizing array of polypeptides.

6. Claims 172-184, 186, 188-192 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of photo lithographic techniques in array synthesis, does not reasonably provide enablement for other techniques (such as chemical, magnetic). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims briefly recite a method of synthesizing a polypeptide array, wherein said array comprises at least two different polypeptides immobilized on a substrate, comprising: a) contacting said surface with a first protected amino acid; b) contacting the said surface with a second protected amino acid; and c) repeating the above steps until at least two different polypeptides are formed at known location on said substrate surface.

The specification disclosure does not have a sufficient enabling disclosure for the use of chemical or thermal or magnetic techniques to remove the protecting groups from the compounds so that activated region on the surface is formed.

The factors to be considered in a determination of undue experimentation are disclosed in *re Wands* (U. S. P. Q. 2d 1400: CAFC 1988) which include: the quantity of experimentation necessary; . the amount of direction or guidance presented; the presence or absence of working examples; the nature of the invention; the state of the prior art; the predictability of the art; and the breadth of the claims.

A number of factors would prevent one of ordinary skill in the art from practicing (making and using) the invention without undue experimentation, which are summarized as follows:

a. The specification fails to give adequate direction and guidance as to the means of synthesizing arrays of polypeptides using techniques other than photolithographic technique. The specification discloses selective deprotection and/or activation with photolithography. The specification discloses that the photolithographic technique makes it possible to direct light to relatively small and precisely known location on the substrate.

b. The working examples directed to the use of photolithographic technique in making arrays of polypeptides or nucleotides.

c. The breadth of the claims are open-ended regarding method of making the arrays.

d. The state of the prior art at the time the invention was made is such that synthesis of array of compounds on a substrate, by selective protecting and deprotecting (using chemical or magnetic methods) in general are known to be difficult or unknown.

e. The art is inherently unpredictable because organic synthesis of peptide array on a substrate and selective protecting and or deprotecting of compounds using chemical or the thermal methods is not possible without using other methods (such as masking using barriers).

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 172-209 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,506,558 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference claims are drawn to a method of forming a plurality of polypeptides or nucleic acids occupying known locations on a substrate, and the reference claim is drawn to both nucleic acid array and polypeptide array. Further the reference does not specifically recite 'array', however "a plurality of polypeptides or nucleic acids occupying known locations on a substrate" reads on the array. The reference method steps are written differently, however the reference method steps are same in scope as the instant claim method steps. Thus, the claimed method is obvious over the reference method.

9. Claims 172-209 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-54 of U.S. Patent No. 6,379,895 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference claims are drawn to a binary synthesis method for synthesizing a plurality

of polypeptides, and the instant claims broadly recite a method of preparing an array of peptides and would read on the reference claims.

Response to Arguments

10. *Applicant's arguments filed on 3/3/04, regarding the written description rejection have been fully considered but they are not persuasive.*

Applicants argue that the teachings of the specification are in no way limited to the use of photolithographic techniques in making arrays, nor is the use of photolithographic techniques critical or essential to practicing the invention. Indeed, the specification specifically exemplifies how photolithography can be used as one deprotection method to selectively activate a positionally defined location on a surface. However, in view of teachings of the specification, it is clear that there are number of alternative activating methods that can be used with similar effect in the instantly claimed method.

Applicants arguments have been fully considered and are not persuasive, because the other means of protecting and deprotecting reagents listed in the specification were not shown use in the claimed method of 'selectively protection or deprotection of reagents on defined locations of the substrate. The specification has a list of reagents which could be used in solid phase chemical synthesis, however, have not shown that the reagents are used or any advantages of the use of the reagents in the claimed method. Further the specification specifically discloses the advantages of the use of the photolithographic technique by reciting in page 10, 'by using lithographic techniques disclosed herein, it is possible to direct light to relatively small and precisely known location on the substrate. It is therefore, possible to synthesize polymers of a known chemical sequence at known locations on the substrate.'

Applicants argue that the working examples involving photolithography demonstrates that the identifying characteristics of selective activation of positionally defined locations on a surface is supplying energy to remove the protecting groups from only the desired area of the surface. In case of photolithography, light serves as energy source. And the specification teaches several energy sources which are suitable for removing protecting groups, it is clear that selective activation of positionally defined locations on a surface can be achieved simply by employing a device or technique analogous to a mask for energy source other that light.

Applicant's arguments regarding the use of 'light' as energy source, and the list of different energy sources disclosed in the specification, have been fully considered and are not persuasive. Since the instant invention is drawn to a method of making polypeptide array using protected amino acids to attach to the activated region of the surface, and not to the inactivated positions on the surface ('light' is used to remove the protecting group from the first selectively activated region of the surface without removing the protecting groups from other positionally defined location of the substrates). The specification has not disclosed the use of any other energy source, which is used in the selectively activating regions of solid support. And the specification further discloses that by using lithographic techniques disclosed herein, it is possible to direct light to relatively small and precisely known location on the substrate. It is therefore, possible to synthesize polymers of a known chemical sequence at known locations on the substrate. The specification nowhere teaches the use of the mask and a different energy source in synthesizing polypeptide array as in the instant claimed method.

Applicants' further argue that the 'because the photolithography examples in the specification are representative of identifying characteristics that are needed to perform the

generic method.' And further applicants argue that it is not necessary to provide working examples for multiple members of a genus when a single genus and there is further description that supports additional methods.

Applicant's arguments have been considered and are not persuasive. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings (or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., Eli Lilly.

In the instant application, the specification has only disclosed the use of 'photolithography techniques' (species) in the polypeptide array synthesis of instant claims. At the time the application was filed the methods of making polypeptides arrays were considered as

unpredictable art. In emerging technologies or in unpredictable art such as 'polypeptide array synthesis', the disclosure of a single species is not representative of the genus. Thus, the claimed invention lacks written description by disclosing only the 'photolithographic methods in polypeptide array synthesis as claimed.'

11. Applicant's arguments filed on 3/3/04, regarding the scope enablement rejection of record have been fully considered but they are not persuasive.

Applicants arguments regarding the 'direction and guidance' in the specification have been considered, and are not persuasive. Applicants argue that 'lithographic techniques' in general are clearly enabled by the specification. And it is apparent from the specification that the photolithography examples are analogous to the methods that would be used with another lithographic techniques. The only requirement is that the mask used be functionally impermeable to the type of radiation being employed.

Applicant's arguments have been considered and are not persuasive. As in the applicants response, the 'photolithographic techniques' are analogous to the other lithographic methods, however the mask has to impermeable to the radiation. However, the specification has not taught the types of masks that can be used with different radiations. And further applicant's arguments 'techniques other than lithography are also enabled by the specification.' However, the specification has not disclosed how the techniques other than lithography are used in the selectively activating regions of the solid surface. Applicant's arguments regarding the 'trenches and V'grooves' are not persuasive, because these limitations would only be useful in maintaining the reagents in certain regions, and not related to the instant claimed method 'selectively activating regions of the solid surface and synthesis of array or polypeptides as claimed.

Applicants arguments regarding the 'magnetic filed' and 'microelectrodes' known at the time the invention was filed, is not persuasive. Because even though the 'magnetic filed' or the 'microelectrodes' are known, they are not related to the chemical synthesis or the prior art has not taught or given motivation to use these different energy sources in solid phase chemical synthesis. Applicants arguments regarding the 'microchips were known and in use (e.g., personal computers) as of the effective filing date of the instant application' are not relevant to the claimed invention. Even though the use of microchip in personal computer industry, it is not known to be any use in chemical array synthesis as claimed at the time the invention was filed or no teachings or guidance for a person in skilled in the art at the time the invention was made to use the microchip techniques in the array synthesis.

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. If little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. In the instant case, the 'polypeptide array synthesis on a solid support by selectively activating selective areas of the surface' is unpredictable. A person skilled in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is lack of predictability in the art.

In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), stated:

[I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof. [Footnote omitted.]

Applicants arguments regarding the method does not lack enablement because a technique is difficult to perform or labor-intensive. Applicants arguments have been considered and are not persuasive, because the amount of experimentation required to adapt the knowledge of different technologies such as 'microchip technology', or microelectronics' or 'magnetic field' in creating the polypeptide arrays as claimed was quite high, especially in light of the specification disclosure of a single example of photolithography techniques in array synthesis, and the advantages of the use of photolithography methods in array synthesis. Thus, for the reasons discussed above the rejections of record have been maintained.

12. Applicant's response filed on 3/3/04 regarding the obviousness type double patenting rejections over US Patent 6,379,895 and US Patent 6,506,558, have been fully considered but they are not persuasive. The rejections of record have been maintained. The rejections would be withdrawn upon filing of terminal disclaimer and entered into the application.

Conclusion

13. No claims are allowed.

14. This is a Continued Examination of applicant's earlier Application No. 09/654,948. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

Pp
26 May 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER